REMARKS

This paper is submitted in response to the Office action dated 31 October 2005 in the above-referenced case.

Claims 6, 8-10, 13-14, 18-19 and 25-26 are canceled without prejudice or disclaimer. Claims 27-36 are added. Therefore, claims 1-2, 15 and 27-36 are pending.

The specification was amended in response to formal objections. Non-elected claims were canceled. Without acquiescing to the 35 U.S.C. §112 and 35 U.S.C. §102 rejections, the independent claims have been amended to more specifically define the VEGF agonist. Claims 27-30 are added which are drawn to the protein and nucleic acid sequences of the VEGF antagonist VEGFR1-R2-FcΔc1(a) (paragraph [0022]). Claims 31-36 are added and drawn to administration by injection, including subcutaneous or intravenous injection. Support is found throughout the specification, for example, at paragraphs 68, 75 (lines 1-3) and 75 (lines 6-9). No new matter is added by these amendments.

In view of such all of the objections and rejections are believed to have been overcome and the application is believed to be in condition for allowance.

I. Formal Matters

A. The specification was objected to for the use of trademarks. In response to the objection, applicants have included specific information with respect to the generic terminology beyond that already present, which information is readily available from a number of published sources. Accordingly, no new matter has been added. Applicants would be amenable to other specific amendments to the specification if the objection is continued. However, the objection is believed to have been overcome.

B. Claims 6, 13 and 18 were objected for encompassing non-elected inventions. Accordingly, claims 6, 13 and 18 are canceled and the elected subject matter incorporated into claims 1 and 15. It is believed this objection may now be withdrawn.

II. Rejections Under 35 U.S.C. § 112, first paragraph

A. Claims 1-2, 8-10, 14-15 and 19 were rejected for lack of enablement. The Examiner states that the specification is "enabling for a method of treating or inhibiting the progression of non-insulin dependent (Type 2) diabetes mellitus (NIDDM) or improving glucose tolerance or insulin sensitivity in a human subject in need thereof comprising administering a VEGF antagonist, wherein the VEGF antagonist is VEGFR1R2-FcΔC1". However, the Examiner does not agree that enablement is provided for "any VEGF antagonist." Further, the Examiner does not find enablement

for administration other than subcutaneous administration or for inhibiting the development of type 2 diabetes.

Although the applicants do not agree with this rejection, in the interest of promoting the progress of the application to issuance, claims 6, 8, 9-10, 13-14, and 18-19 are canceled, and claims 1 and 15 are amended to limit the VEGF antagonist to VEGFR1R2-FcΔ1(a).

Regarding the method of administration, it is respectfully submitted that the VEGF antagonist VEGFR1R2-FcΔ1(a) has been shown to be effective in human subjects to treat a variety of conditions when administered subcutaneously or intravenously. The experiments described in the instant specification appropriately comprise administration of VEGFR1R2-FcΔ1(a) to diabetic (*db/db*) mice by subcutaneous injection.

The Examiner has correctly pointed out that there is some degree of unpredictability with respect to obtaining a particular desired therapeutic result when using different means of administration. However, the Examiner will understand that the action of the VEGF antagonist depends on its presence in the circulation, which reflects its bioavailability (pK). Applicants have conducted pharmacokinetic studies which establish that bioavailability of the VEGF trap is achieved by intravenous, intraperitoneal, intravitreal, or subcutaneous injection. Applicants are not attempting to obtain FDA approval with respect to each and every means of administration. However, applicants have clearly demonstrated operability with respect to a particular means of administration. Based on the ability of the VEGF antagonist of the invention to bind VEGF, it is respectfully submitted that any method of administration which allows the VEGF antagonist to be present in the systemic circulation would be expected to obtain the desired therapeutic result. That therapeutic result may vary depending upon the means of administration and the amount of dosing may vary depending on the means of administration. However, such does not render applicants' invention as not being enabled as indicated within the rejection. Further, applicants' position with respect to this matter is strengthened by applicants specifically identifying the VEGF antagonist which is administered in that the affinity of the VEGF antagonist for endogenous VEGF has been clearly demonstrated by applicants. In view of such, reconsideration and withdrawal of the rejection is respectfully requested.

B. Claims 1-2, 8-10, 14-15 and 19 were rejected for lack of written description. The Examiner found written description support for VEGF inhibitors Flt-1(1-3), Flt-1(1-$3_{R->N}$)-Fc, Flt-1(1-$3_{\Delta B}$)-Fc, Flt-1(2-$3_{\Delta B}$)-Fc, Flt-1(2-3)-Fc, Flt-1D2-VEGFR3D3-FcΔC1(a), Flt-1D2-Flk-1D3-FcΔC1(a), and VEGFR1R2-FcΔC1(a), but not for all VEGF antagonists. It is believed that this rejection is rendered moot by the above amendments and may now be withdrawn.

III. Rejections Under 35 U.S.C. § 112, second paragraph.

A. Claims 1, 9 and 15 were rejected as indefinite for recitation of the term "VEGF-mediated activity." Claim 9 is canceled. Claims 1 and 15 are amended to delete the phrase "an agent capable of blocking, inhibiting, or ameliorating VEGF-mediated activity such that diabetes is treated, wherein the agent is". Accordingly, it is believed this rejection may now be withdrawn.

B. Claims 2 and 10 were rejected as indefinite for recitation of the term "glycemic control." Claim 10 is canceled. Claim 2 is amended to delete the term. Accordingly, this rejection may now be withdrawn.

C. Claim 15 was rejected as indefinite on the basis that the claim does not have a step that clearly relates back to the preamble. In response, claim 15 is amended to insert "such that glucose tolerance or insulin sensitivity is improved". Accordingly, this rejection may now be withdrawn.

D. Claims 6, 8, 13-14, and 18-19 were rejected for depending on an indefinite claim. This rejection is rendered moot by cancellation of the claims.

IV. Rejections Under 35 U.S.C. § 102(e).

Claims 1, 8-9, 14-15, and 19 were rejected as anticipated by Thorpe et al. (U.S. Patent No. 6,524,583). It is believed that this rejection is rendered moot by the above amendments to the claims.

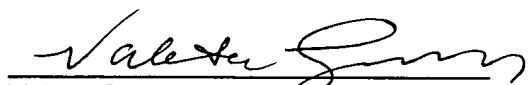
Conclusion

It is believed that this document is fully responsive to the Office action dated 31 October 2005. It is believed that the claims are now in condition for allowance, and such action is respectfully urged.

Fees

Although it is believed that no fees are due, in the event the Patent Office determines that fees are due, the Commissioner is hereby authorized to charge Deposit Account Number 18-0650 in the amount of any fees deemed to be due.

Respectfully submitted



Valeta Gregg, Ph.D., Reg. No. 35,127
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, New York 10591
(914) 345-7400 (914-593-1077 direct)